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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,840	02/27/2004	Thomas J. Meade	A-67277-5/RMS/RMK	8243

67374 7590 07/12/2007

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EXAMINER	
SCHLIENTZ, LEAH H	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
07/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,840	MEADE, THOMAS J.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *5-9 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10-15 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *2/27/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 4/27/07 is acknowledged. The traversal is on the ground(s) that a macrocyclic and acyclic chelators are not unconnected in operation, that claim 1 is a linking claim which is generic to both cyclic and acyclic chelators, and that a reasonable number of particular species are presented. This is not found persuasive. The restriction requirement is maintained for reasons of record. For example, Groups I and II are drawn to chemically distinct chelators, and have acquired a separate subclass in the art. Searching all chelators, macrocyclic and acyclic would require a search extending over various classes and subclasses, as well as non-patent literature, and it would constitute and undue burden to search all of the grouped inventions. Furthermore, "Where an application includes claims to distinct inventions as well as linking claims, restriction can nevertheless be required." See MPEP 809. The linking claims must be examined with, and thus are considered part of, the invention elected. When all claims directed to the elected invention are allowable, should any linking claim be allowable, the restriction requirement between the linked inventions must be withdrawn. Any claim(s) directed to the nonelected invention(s), previously withdrawn from consideration, which depends from or requires all the limitations of the allowable linking claim must be rejoined and will be fully examined for patentability. Where the requirement for restriction in an application is predicated upon the nonallowability of generic or other type of linking

claims, applicant is entitled to retain in the application claims to the nonelected invention or inventions. Where such withdrawn claims have been canceled by applicant pursuant to the restriction requirement, upon the allowance of the linking claim(s), the examiner must notify applicant that any canceled, nonelected claim(s) which depends from or requires all the limitations of the allowable linking claim may be reinstated by submitting the claim(s) in an amendment. Upon entry of the amendment, the amended claim(s) will be fully examined for patentability. The requirement is still deemed proper and is therefore made FINAL. Acknowledgement is also made to the election of the following species: doxorubicin as an agent therapeutically active in cancer, and carbohydrate/carbohydrase as cleavage site and enzyme. Claims 1 - 17 are pending, of which claims 5 - 9 and 16 are withdrawn from consideration as being drawn to non-elected species. Claims 1 - 4, 10 - 15 and 17 are readable upon the elected invention and species and have been examined on the merits for patentability.

Priority

This application claims priority to multiple provisional applications. Claim is made as a continuation to US 09/716,175, which claims benefit to US 60/201,817 and US 60/203,224, and as a continuation-in-part to US 09/179,927 (now US 6,713,046), which claims benefit to US 60/063,328. It is noted that support for the concept of an agent therapeutically active in cancer was not found in the '927 or '328 applications. As such, the priority date for the full scope of the instant claims was determined to be the filing date of the '817 application, or 5/4/2000.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 - 4 are 11 - 15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 16 of U.S. Patent No. 6,713,046, in view of Snow *et al.* (US 5,932,188). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method comprising a) administering an MRI agent comprising a chelating agent, a paramagnetic metal ion, a cleavage site (as in the case of the instant application) or a photocleavable moiety (as in the '046 patent), and a therapeutic blocking moiety; b) cleaving a therapeutic blocking moiety; and c) producing a magnetic resonance image of a cell, tissue, or patient and eliciting a therapeutic effect. The photocleavage step of the '046 application is anticipatory of the instantly claimed

generic cleaving step. While the '046 patent does not specifically require that the "therapeutic blocking moiety" is therapeutically active in cancer, it would have been obvious to one of ordinary skill in the art that a therapeutic moiety which is conjugated to a chelator via a linker may be an anticancer agent, as taught by Snow. Snow discloses that a cytotoxic agent, such as a chemotherapeutic agent, may be covalently bonded to a chelating agent or a linking group, and that the inherent cytotoxic properties of the agent are maintained or regenerated as a result of cleavage of such a bond (column 2, lines 42+). Accordingly, the claims are overlapping in scope and are obvious variants of one another.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims appear to contain a typographical error. The claim is drawn to a method according to claim 1, wherein said cleavage site comprises a carbohydrate group capable of being cleaved by a carbohydrate. It is interpreted, based on the Response filed 4/27/2007, that the second occurrence of "carbohydrate" was intended to read "carbohydrase," which was elected on page 5 of the Response.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 – 4, 10 – 15 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Snow *et al.* (US 5,932,188).

Snow discloses that the concept of drug targeting has gained importance in recent years, especially for anticancer drugs, inasmuch as toxic side effects of anticancer drugs to normal cells are a primary obstacle in cancer chemotherapy due to the lack of selectivity to cancer cells. Reactive poly(alkylene oxides) can be contacted with chelating agents or precursors thereof containing reactive functionality to form targeting polymers which, when associated with cytotoxic agents, find particular utility in therapeutic and diagnostic imaging compositions and methods (column 1, lines 25 – 60). The cytotoxic agent is an agent able to kill cells, including chemotherapeutic agents, which can be covalently bound to a chelating agent or to a linking group. The inherent cytotoxic properties of the agent are maintained or regenerated as a result of cleavage of said bonds (column 2, lines 42+). Preferred residues of chelating agents include DOTA (column 4, lines 35+). Regarding claims 12 – 14, the residue of the chelating agent is linked to the polymer through a chemical bond or linking group, which include a nitrogen atom, alkyl group, including those containing from 1 to 18 carbons being interrupted by one or more heteroatoms, such as oxygen (column 5, lines 47+).

The cytotoxic agent may include doxorubicin (column 7, line 39). The polymer may include both a therapeutic moiety and a moiety for enhancing contrast during MR imaging. For MR imaging applications, the metal ion chelated by the chelator (M^{+a}) may include Cr^{3+}, Fe^{3+}, Gd^{3+}, Dy^{3+} (column 8, lines 51+). The cytotoxic agents are covalently linked to the polymer or the chelating group or to elements of the linking group by a variety of chemical bonds or linking groups (column 11, lines 9 – 15). In some embodiments, the polymer can contain an immunoreactive group covalently bonded thereto. Such an immunoreactive group has a capacity for interaction with another component which may be found in biological fluids or associated with cells to be treated such as tumor cells, and may include polysaccharides, carbohydrates, etc. (column 11, lines 60 – column 12, line 16). The compositions can be administered orally, intravenously, etc. (column 14, line 35).

Regarding claim 1, a composition comprising a chelator and a paramagnetic metal ion for MR imaging, a poly(alkylene oxide) polymer, a linker and a cytotoxic agent are be administered. The composition must inherently comprise a "cleavage site" and thus a cleavage step upon in vivo administration, as claimed, because Snow teaches that the inherent cytotoxic properties of the cytotoxic agent are maintained or regenerated as a result of cleavage of covalent bonds which link the cytotoxic agent to the chelating agent, linker, or polymer (column 2, lines 42+). The recitation of such functional properties, such as a decrease in the T_1 of the MRI agent, must also necessarily occur, since the same compositions must have the same properties. Regarding claims 10 and 17, the composition may further comprise a polysaccharide or

carbohydrate group, and thus must inherently be "capable of" being cleaved by a carbohydrate, as claimed. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LHS

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER